

Compound 3

49% yield, 2 steps; NMR d (CD₃SOCD₃) 2.27 (s, 3H), 2.54 (t, 4H), 2.62 (t, 4H), 3.22 (s, 2H),
5 5.84 (s, 2H), 6.95 (dd, 1H), 7.22 (m, 2H), 7.33 (s, 1H), 7.41 (s, 1H), 7.50 (d, 1H), 7.72 (d,
1H), 9.75 (s, 1H); *M/z* (-) 475 (*M*⁻), 473, 429, 109.

Compound 6

14% yield, 2 steps; *M/z* (-) 510 (*M*⁻), 508, 464.

Example 3**Di-ester of Compound 8**

Ethyl 4-chloroacetamido-*N*-(3,4-dichlorobenzyl)indole-2-carboxylate (0.4 g), glycine
methyl ester hydrochloride (0.57 g) and triethylamine (1.25 ml) were dissolved in
15 methoxyethanol (4.0 ml) and the reaction heated at 100°C for 6 hours. The reaction was
cooled and partitioned between water and ethyl acetate. Combined organic extracts were
dried (MgSO₄) and concentrated and the residue purified by chromatography using toluene :
ethyl acetate (1:1) as eluent to give the product, ethyl 4-[(*N*-(methoxycarbonylmethyl)-
glycyl)amino]-*N*-(3,4-dichlorobenzyl)indole-2-carboxylate, as a pale yellow solid (0.17 g,
20 38%); NMR d (CD₃SOCD₃) 1.28 (t, 3H), 3.44 (s, 2H), 3.50 (s, 2H), 3.63 (s, 3H), 4.28 (q, 2H),
5.82 (s, 2H), 6.88 (dd, 1H), 7.10 - 7.30 (m, 4H), 7.50 (d, 1H), 7.69 (s, 1H), 7.80 (dd, 1H),
10.00 (brs, 1H); *M/z* (+) 494, 492 (*M*⁺).

Example 4**Di-ester of Compound 11**

Methanesulphonyl chloride (0.1 ml) was added to stirred solution of ethyl 4-[(*N*-
(methoxycarbonylmethyl)glycyl)amino]-*N*-(3,4-dichlorobenzyl)indole-2-carboxylate (0.33 g)
and triethylamine (0.47 ml) in dichloromethane (4.0 ml) and the reaction stirred for 3 hours.
The reaction was poured into water and extracted with ethyl acetate. Combined organic
30 extracts were dried (MgSO₄) and concentrated and the residue triturated with ether, filtered
and dried *in vacuo* to give the product as a white solid (0.24 g, 63%); NMR d (CD₃SOCD₃)

1.27 (t, 3H), 3.10 (s, 3H), 3.67 (s, 3H), 4.20 (s, 2H), 4.28 (q+s, 2H+2H), 5.82 (s, 2H), 6.87 (dd, 1H), 7.28 (m, 3H), 7.50 (d, 1H), 7.80 (m, 2H), 10.00 (brs, 1H); M/z (+) 572, 570 (M^+).

5 Example 5

The procedure described in the Example 4 above was repeated using the appropriate acid chloride. Thus was obtained the compound described below.

Di-ester of Compound 12

10 64% yield; M/z (-) 534 (M^+), 532.

Example 6

Di-ester of Compound 14

Sarcosine ethyl ester hydrochloride (1.23 g) and potassium carbonate (1.11 g) were
15 added to a solution of ethyl 4-chloroacetamido-*N*-(3,4-dichlorobenzyl)indole-2-carboxylate (700 mg) in acetone (25 ml), stirred and heated at 65°C overnight. The reaction was partitioned between water (50 ml) and ethyl acetate (50 ml), extracted with ethyl acetate (2 x 50 ml), and dried ($MgSO_4$). The combined organic extracts were concentrated *in vacuo*, and the residue purified by column chromatography using 30% ethyl acetate : toluene as eluent, to
20 afford the product as a yellow solid (768 mg, 92%); NMR d (CD_3SOCD_3) 1.21 (t, 3H), 1.28 (t, 3H), 2.45 (s, 3H), 3.42 (s, 2H), 3.53 (s, 2H), 4.16 (q, 2H), 4.30 (q, 2H), 5.81 (s, 2H), 6.88 (d, 1H), 7.27 (m, 2H), 7.52 (d, 1H), 7.67 (s, 1H), 7.84 (d, 1H), 9.95 (s, 1H), M/z (+) 520.3 (MH^+)

Example 7

25 The procedure described in Example 6 above was repeated using the appropriate amine. Thus was obtained the compound described below.

Diester of Compound 13

93% yield; NMR d (CD_3SOCD_3) 1.15 (t, 3H), 1.28 (t, 3H), 3.52 (s, 3H), 3.57 (s, 3H), 3.87 (s, 2H), 4.10 (q, 2H), 4.31 (q, 2H), 5.83 (s, 2H), 6.90 (d, 1H), 7.15 - 7.44 (m, 8H), 7.53 (d, 1H),
30 7.67 (s, 1H), 7.83 (d, 1H); M/z (+) 596.5 (MH^+).

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Example 8**5 Di-ester of Compound 15**

A solution of methyl iodide (0.026 ml) in DMF (2 ml) was added to a solution of sodium hydride (15 mg, 60% in mineral oil) and ethyl 4-[(*N*-benzyl-*N*-ethoxycarbonylmethyl)glycyl]amino-*N*-(3,4-dichlorobenzyl)indole-2-carboxylate (the diester of Compound 13) (200 mg) in DMF (4 ml), and stirred under an atmosphere of argon at ambient temperature for 4 hours. The reaction was quenched with water (50 ml) and extracted with ethyl acetate (3 x 50 ml), and the combined organic extracts were dried (MgSO₄), and concentrated *in vacuo* to afford the product as a pale brown oil (93 mg, 45%); NMR d (CD₃SOCD₃) 1.05 (t, 3H), 1.30 (t, 3H), 3.21 (s, 2H), 3.28 (s, 3H), 3.41 (s, 2H), 3.70 (s, 2H), 3.93 (q, 2H), 4.30 (q, 2H), 5.84 (s, 2H), 6.90 (d, 1H), 7.01 (d, 1H), 7.07 - 7.40 (m, 8H), 7.48 - 7.64 (m, 2H); *M/z* (+) 610.5 (*MH*⁺).

Example 9**Compound 8**

Ethyl 4-[(*N*-(methoxycarbonylmethyl)glycyl)amino]-*N*-(3,4-dichlorobenzyl)indole-2-carboxylate (0.15 g) was dissolved in THF / methanol (1:1) (10 ml) and sodium hydroxide (2M, 2.5 ml) was added and the reaction stirred for 16 hours. The reaction was then concentrated *in vacuo* and the residue dissolved in water. The solution was acidified by dropwise addition of acetic acid, resulting in the precipitation of a white solid which was filtered, washed with water and dried *in vacuo* to give the desired end product as a white solid (108 mg, 79%); NMR d (CD₃SOCD₃) 3.40 (s, 2H), 3.64 (s, 2H), 5.82 (s, 2H), 6.92 (dd, 1H), 7.20 - 7.38 (m, 3H), 7.50 (d, 1H), 7.62 (s, 1H), 7.78 (d, 1H), 10.15 (brs, 1H).

Example 10

The procedure described in Example 9 above was repeated using the appropriate ester. Thus were obtained the compounds described below.